APS Search for 08/948,393
FILE 'USPAT' ENTERED AT 16:24:44 ON 08 APR 1998

=> s selectin or sclectins or elam or padgem

231 SELECTIN
150 SELECTINS
303 ELAM
79 PADGEM
L1 467 SELECTIN OR SELECTINS OR ELAM OR PADGEM

=> s atherosclerosis or arteriosclerosis

4452 ATHEROSCLEROSIS
2932 ARTERIOSCLEROSIS
L2 6381 ATHEROSCLEPOSIS OR ARTERIOSCLEROSIS

=> s l1 (p) l2

L3 13 L1 (P) L2

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US PAT NO: 5,719,268 [IMAGE AVAILABLE] L3: 1 of 13
DATE ISSUED: Feb. 17, 1998
TITLE: Endothelial cell adhesion molecules
INVENTOR: Leslie M. McEvoy, Mountain View, CA
Eugene C. Butcher Portola Valley, CA
ASSIGNEE: The Board of Trustees of the Leland Junior Stanford University, Palo Alto, CA (U.S. corp.)
APPL-NO: 08,338,938
DATE FILED: Nov. 14, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 111,827, Aug. 25, 1993, abandoned, which is a continuation of Ser. No. 864,603, Apr. 7, 1992, abandoned.
INT-CL: [6] C07K 16/18; C07K 16/28, C12N 5/12
US-CL-ISSUED: 530/388.22, 388.1, 388.2, 435/332, 334
US-CL-CURRENT: 530/388.22; 435/332, 334; 530/388.1, 388.2
SEARCH-FLD: 435/70.21, 172.2, 740.27, 326, 332, 334; 530/388.1, 388.22, 389.5 388.2
REF-CITED:

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Lewinsohn, et al , (1987) J. Immunology 138:4313.
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Territo, et al., (1989) Arteriosclerosis 9:824.
ART-UNIT: 186
PRIM-EXMR: Paula K. Hutzell
ASST-EXMR: Phillip Gambel
LEGAL-REP: Pamela J Bozicevic & Reed LLP Sherwood

ABSTRACT:
Methods and compositions are provided for the modulation of monocyte binding to endothelial cells particularly during inflammatory episodes. Compositions are provided which bind to one or both of the monocyte surface membrane protein or the endothelial surface membrane protein which are complementary or result in the adhesion of the monocyte to the endothelial cell. The subject compositions can be used in diagnosis or therapy

2 Claims, No Drawings

US PAT NO: 5,719,268 [IMAGE AVAILABLE] L3: 1 of 13

SUMMARY:

BSUM(9)

Jutila . . . et al., Blood 77:2266 report the binding of human monocytes to two cytokine-induced adhesive ligands on cultured human endothelial cells: **ELAM**-2 and VCAM-1. See also Cybulski and Gimbrone (1991) Science 251:788. Gerrity (1981) Am. J. Pathol. 103:181 describes the role of . . . J. Cellular Biochem. 45:156 describes GMP-140 as a receptor for monocytes on activated platelets and endothelium. Territo et al. (1989) **Arteriosclerosis** 9:824 report that BVLDL pretreatment of endothelial monolayers increases monocyte adhesion.

US PAT NO: 5,712,274 [IMAGE AVAILABLE] L3: 2 of 13
DATE ISSUED: Jan. 27, 1998
TITLE: Thienotriazolodiazepine compounds and their pharmaceutical use
INVENTOR: Hiroyuki Sueoka, Fukuoka, Japan
Shuji Ehara, Fukuoka, Japan
Haruhito Kobayashi Fukuoka Japan
Takeshi Arichi, Fukuoka, Japan
Hirotsuga Komatsu, Saitama, Japan
ASSIGNEE: Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (foreign corp.)
APPL-NO: 08/413,444
DATE FILED: Mar. 30, 1995
REL-US-DATA: Continuation-in-part of Ser. No. 403,726, Mar. 17, 1995, abandoned.
INT-CL: [6] A61K 31/55, C07D 243/06
US-CL-ISSUED: 514/219, 220; 540/555, 560
US-CL-CURRENT: 514/219, 220; 540/555, 560
SEARCH-FLD: 540/855, 560; 514/219, 220
REF-CITED:

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Derwent Abstract of DE-3936828 corresponding to JP-A-243691 (1989).
Derwent Abstract of DE-4006471 corresponding to JP-A-2-275883 (1990).
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Derwent Abstrct of JP-A-297479 (1993).
Derwent Abstract of WO89/05812 (1989).
Derwent Abstract of WO93/12117 (1993).
Derwent Abstract of WO94/22872 (1994).
Derwent Abstract of WO93/07129 (1993).
ART-UNIT: 122
PRIM-EXMR John M. Ford
ASST-EXMR Brenda Coleman
LEGAL-REP: Wenderoth, Lind & Ponack

ABSTRACT:
Thienotriazolodiazepine compounds of the formula (I) ##STR1## wherein each symbol is as defined in the specification, pharmaceutically acceptable salts thereof, and pharmaceutical use thereof. The compounds of the present invention are useful as preventive and therapeutic drugs for inflammatory diseases and allergic diseases, in which cell adhesion is involved.

12 Claims, No Drawings

US PAT NO: 5,712,274 [IMAGE AVAILABLE] L3: 2 of 13

SUMMARY:

BSUM(8)

In connection with diseases, promoted expressions of ICAM-1 and **ELAM**-1 in inflammatory sites in autoimmune diseases such as inflammatory skin diseases (e.g. contact dermatitis, light eruptions caused by high photosensitivity . . . nephritis and so on. Moreover, cell adhesion molecules are known to be deeply involved in the formation and evolution of **atherosclerosis**, ischemia-reperfusion injury, septic shock and so on.

US PAT NO: 5,710,123 [IMAGE AVAILABLE] L3: 3 of 13
DATE ISSUED: Jan. 20, 1998
TITLE: Peptide inhibitors of selectin binding
INVENTOR: George A. Heavner, Malvern, PA
Marian Krupczynski, King of Prussia, PA
ASSIGNEE: Centocor, Inc., Malvern, PA (U.S. corp.)
APPL-NO: 08/454,207
DATE FILED: Jun. 9, 1995
PCT-FILED: Dec. 13, 1993
PCT-NO: PCT/US93/12110
371-DATE: Jun. 9, 1995
102(E)-DATE Jun. 9, 1995
PCT-PUB-NO: WO94/14836
PCT-PUB-DATE: Jul. 7, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 997,771, Dec. 18, 1992, abandoned.
INT-CL: [6] A01N 37/18, A61K 38/00; C07K 5/00; C07K 7/00
US-CL-ISSUED: 514/2, 9, 15; 530/300, 317, 321, 328, 333, 334
US-CL-CURRENT: 514/2, 9, 15; 530/300, 317, 321, 328, 333, 334

SEARCH FIELD 514/2, 9, 15; 530/300, 317, 321, 328, 333, 334

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WO 91/19502	12/1991 World Intellectual Property Organization
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Yong, K. and Khwaja, A., "Leucocyte cellular adhesion molecules", Blood Reviews 1990, 4, 21-225.
ART-UNIT: 187
PRIM-EXMR: W. Gary Jones
ASST-EXMR: Amy Atzel
LEGAL-REP: Woodcock Washburn Kurtz Mackiewicz & Norris LLP

ABSTRACT:

The present invention provides novel peptides having as their core region portions of the 109-118 amino acid sequence of P-selectin, E-selectin or L-selectin. The invention also provides pharmaceutical compositions comprising the peptides of the invention, and diagnostic and therapeutic methods utilizing the peptides and pharmaceutical compositions of the invention.

23 Claims, No Drawings

US PAT NO: 5,710,123 [IMAGE AVAILABLE] L3: 3 of 13

SUMMARY:

BSUM(110)

Tumor ... has been well described, suggesting a role for platelets in the spread of some cancers. Recently, it was reported that P-**selectin** binds to tumor cells in a variety of human carcinoma tissue sections (colon, lung, and breast), and that P-**selectin** binds to the cell surface of a number of cell lines derived from various carcinomas, but not from melanomas. Aruffo, ... A., et al., Proc. Natl. Acad. Sci. USA, 89, 2292-2296 (1992). Aruggo et al also reference earlier work suggesting that E-**selectin** might be involved in tumor metastasis by mediating the adhesion of a colon carcinoma cell line (HT-20) to activated endothelial cells in vitro. Platelet-leukocyte interactions are believed to be important in **atherosclerosis**. Platelets might have a role in recruitment of monocytes into atherosclerotic plaques; the accumulation of monocytes is known to be. .

US PAT NO: 5,708,147 [IMAGE AVAILABLE] L3: 4 of 13
DATE ISSUED: Jan. 13, 1998
TITLE: Mononuclear leukocyte directed endothelial adhesion molecule associated with atherosclerosis
INVENTOR: Michael A. Gimbrone, Jr., Boston, MA
Myron I. Cybulsky, Allston, MA
Tucker Collins, Cohasset, MA

ASSIGNEE: Brigham & Women's Hospital, Boston, MA (U.S. corp.)
APPL-NO: 08/261,304
DATE-FILED: Jun. 16, 1994
REL-US-DATA: Continuation of Ser. No. 649,565, Feb. 1, 1991, abandoned, which is a continuation-in-part of Ser. No. 487,038, Mar. 2, 1990, abandoned
INT-CL: [6] C07K 14/00
US-CL-ISSUED: 530/388.7; 350; 395; 436/63; 86
US-CL-CURRENT: 530/388.7; 436/63; 86, 530/350; 395
SEARCH-FLD: 530/350; 388.7; 380; 395; 436/63; 86
REF-CITED:

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5,081,034 1/1992 Bevilacqua et al. 435/252

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0408859A2 1/1991 European Patent Office
WO9013300 11/1990 World Intellectual Property Organization

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Young et al. Proc. Natl. Acad. Sci. USA, vol. 80, pp. 1194-1198, Mar. 1983.
ART-UNIT: 183
PRIM-EXMR: Christine M. Nucker
ASST-EXMR: Laurie Scheiner
LEGAL-REP: Sterne, Kessler, Goldstein & Fox

ABSTRACT:
The invention relates to novel endothelial cell-leukocyte adhesion molecules designated ATHERO-**ELAM**. ATHERO-**ELAM** molecules are expressed on cultured endothelial cells stimulated with bacterial LPS and selectively mediate the binding of monocytes to the endothelial cells. Monoclonal antibodies specific for ATHERO-**ELAM** bind to vascular endothelial cells involved in early atherosclerotic lesions, but not to vascular endothelial cells from uninvolved arterial tissue. ATHERO-**ELAM** and antibodies directed to ATHERO-**ELAM** may be used in identifying early atherosclerotic lesions and in treating and preventing **atherosclerosis**

5 Claims, 29 Drawing Figures

US PAT NO: 5,708,147 [IMAGE AVAILABLE] L3: 4 of 13

ABSTRACT:
The invention relates to novel endothelial cell-leukocyte adhesion molecules designated ATHERO-**ELAM**. ATHERO-**ELAM** molecules are expressed on cultured endothelial cells stimulated with bacterial LPS and selectively mediate the binding of monocytes to the endothelial cells. Monoclonal antibodies specific for ATHERO-**ELAM** bind to vascular endothelial cells involved in early atherosclerotic lesions, but not to vascular endothelial cells from uninvolved arterial tissue. ATHERO-**ELAM** and antibodies directed to ATHERO-**ELAM** may be used in identifying early atherosclerotic lesions and in treating and preventing **atherosclerosis**.

SUMMARY:

BSUM(13)

The . . . and are markers for early atherosclerotic lesions in blood vessels. The invention also relates to monoclonal antibodies specific for an ATHERO-**ELAM** and uses of these monoclonal antibodies in diagnosis of **atherosclerosis** and in intervention during its progression. The invention further relates to the use of soluble forms of ATHERO ELAMs to intervene with the progression of **atherosclerosis**

DETDESC:

DETD(3)

By "ATHERO-**ELAM**" is meant an endothelial cell surface protein expressed at sites of oligo ng/active **atherosclerosis** which participates in leukocyte-endothelial adhesion.

US PAT NO: 5,693,621 [IMAGE AVAILABLE] L3: 5 of 13
DATE ISSUED: Dec. 2, 1997
TITLE: Malonic acid derivatives having antiadhesive properties
INVENTOR: Alexander Toepfer, Hofheim, Federal Republic of Germany
Gerhard Kretzschmar, Eschborn, Federal Republic of Germany
Eckart Bartnik, Wiesbaden, Federal Republic of Germany
Dirk Seiffge, Mainz-Kostheim, Federal Republic of Germany
ASSIGNEE: Hoechst Aktiengesellschaft, Frankfurt am Main, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/403,525
DATE FILED: Mar. 13, 1995
FRN PRIOR: Federal Republic of Germany44 08 248.7 Mar. 11, 1994
Federal Republic of Germany44 30 005.0 Aug. 25, 1994
INT-CL: [6] A61K 31/19; A61K 31/70; C07C 55/00, C07H 15/00
US-CL-ISSUED: 514/25, 574; 536/4.1; 562/400, 590
US-CL-CURRENT: 514/25, 574, 536/4.1; 562/400, 590
SEARCH-FLD: 536/4.1; 562/400, 590; 514/25, 574, 557
REF-CITED:

U.S. PATENT DOCUMENTS

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5,162,513	11/1992	Wong	536/1.1

FOREIGN PATENT DOCUMENTS

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WO 92/00251	1/1992	World Intellectual Property Organization
WO 92/00245	1/1992	World Intellectual Property Organization
WO 92/09870	6/1992	World Intellectual Property Organization
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0 536 394	4/1993	World Intellectual Property Organization

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ART-UNIT: 121
PRIM-EXMR: Elli Peselev
LEGAL-REP: Foley & Lardner

ABSTRACT:

The invention relates to malonic acid derivatives, which inhibit the binding of selectin to carbohydrate ligands, and pharmaceutical compositions and diagnostic agents containing these derivatives, and methods for using these pharmaceutical compositions and diagnostic agents.

20 Claims, No Drawings

US PAT NO: 5,693,621 [IMAGE AVAILABLE] L3: 5 of 13

SUMMARY:

BSUM(4)

Compounds . . . such as rheumatoid arthritis, asthma, and psoriasis.

Other indications include adult respiratory distress syndrome, reperfusion injury, ischemia, ulcerative colitis, vasculitis, **atherosclerosis**, and inflammatory bowel disease. (Boschelli et al., U.S. Pat. No. 5,356,926). Synthetic analogs (mimetics) of carbohydrate ligands that bind specifically to **selectins**, and thus inhibit **selectin**-mediated intercellular adhesion, have been implicated as promising therapeutics as anti-inflammatories and anti-coagulants (T. A. Springer, L. A. Lasky, Nature 349, .

US PAT NO: 5,632,991 [IMAGE AVAILABLE] L3: 6 of 13
DATE ISSUED: May 27, 1997
TITLE: Antibodies specific for L-selectin and the uses thereof
INVENTOR: Michael A. Gimbrone, Jr., Jamaica Plain, MA
ASSIGNEE: Brigham & Women's Hospital, Boston, MA (U.S. corp.)
APPL-NO: 08/365,470
DATE FILED: Dec. 29, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 102,510, Aug. 5, 1993, Pat. No. 5,403,713, which is a continuation of Ser. No. 850,802, Mar. 13, 1992, abandoned, which is a division of Ser. No. 270,860, Nov. 14, 1988, abandoned.
INT-CL: [6] A61K 39/395; A61K 39/44; C07K 16/28
US-CL-ISSUED: 424/178.1, 143.1, 172.1; 530/395, 391.7
US-CL-CURRENT: 424/178.1, 143.1, 172.1; 530/391.7, 395
SEARCH-FLD: 424/152.1, 172.1, 178.1, 143.1; 530/388.22, 389.1, 391.1, 391.7
REF-CITED:

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5,081,034	1/1992	Bevilacqua et al.	435/252.33
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ART-UNIT: 186
PRIM-EXMR: Thomas M. Cunningham
LEGAL-REP: Sterne, Kessler, Goldstein & Fox, PLLC

ABSTRACT:
A method is provided for selectively targeting a therapeutic agent to a site of activated endothelium by administering a pharmaceutical composition comprising a therapeutically effective amount of an E-selectin (formerly called ELAM-1) specific monoclonal antibody conjugated to a therapeutic agent. An immunoconjugate comprising an E-selectin specific monoclonal antibody and a therapeutic agent is also provided. A method is also provided for the treatment of a vascular smooth muscle cell proliferative disorder, vasculitis, inflammation, post-reperfusion injury, microbial infections, acute or chronic allograft rejection, and leukemia, as well as for the inhibition of metastatic spread of tumor cells, by administering a pharmaceutical composition comprising a therapeutically effective amount of an E-selectin antibody, or antibody fragment, either alone, or conjugated to a therapeutic agent.
15 Claims, 13 Drawing Figures

US PAT NO: 5,632,991 [IMAGE AVAILABLE] L3: 6 of 13

DETDESC:

DETD(46)

By "smooth muscle cell proliferative disorder" is meant a disorder, such as **atherosclerosis** or post angioplasty restenosis, that is characterized by the proliferation of smooth muscle cells. Both **atherosclerosis** and post-angioplasty restenosis are characterized by cytokine-activated vascular endothelial cells that express E-**selectin** on the cell surface. When vascular endothelium is damaged, as in these states, thrombin occupies receptors on the endothelium and. . . Biol. 103:1129-1133 (1986)). Thrombin generation is predicted to be an important component of vascular "response to injury" processes such as **atherosclerosis** and post-angioplasty restenosis. Thus, the invention relates to the specific targeting of an anti-smooth cell proliferative agent, such as an. . . agent or an anti-platelet derived growth factor, to the site of proliferation or migration of smooth muscle cells (i.e., in **atherosclerosis** or post-angioplasty restenosis) by conjugating the agent to an E-**selectin** specific monoclonal antibody.

US PAT NO: 5,618,785 [IMAGE AVAILABLE] L3: 7 of 13
DATE ISSUED: Apr. 8, 1997
TITLE: Peptide inhibitors of selectin binding
INVENTOR: George A. Heavner, Malvern, PA
Marian Kruszynski, West Chester, PA
Miljenko Mervic, King of Prussia, PA
ASSIGNEE: Centocor, Inc., Malvern, PA (U.S. corp.)
APPL-NO: 08/457,804
DATE FILED: Jun. 1, 1995
REL-US-DATA: Continuation of Ser. No. 156,415, Nov. 22, 1993, abandoned.
INT-CL: [6] A61K 38/08; C07K 7/06
US-CL-ISSUED: 514/2; 530/328
US-CL-CURRENT: 514/2; 530/328
SEARCH-FLD: 530/328; 514/16.2
REF-CITED:

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5,08..,034	1/1992	Bevilacqua et al.	435/252.33
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5,227,369	7/1993	Rosen et al.	514/23
5,378,464	1/1995	McEver	424/143.1
5,440,015	8/1995	Macher et al.	530/329
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WO91/19502	12/1991 World Intellectual Property Organization
WO91/19501	12/1991 World Intellectual Property Organization
WO92/01718	2/1992 World Intellectual Property Organization
WO92/02527	2/1992 World Intellectual Property Organization

ART-UNIT: 187
PRIM-EXMR: Kenneth R. Horlick
LEGAL-REP: Woodcock Washburn Kurtz Mackiewicz & Norris

ABSTRACT:
The present invention provides novel peptides constructed to mimic the topology of the surface exposed segements of the 23-30 sequence and Tyr sup.118 in the lectin domain of P-selectin. The invention also provides pharmaceutical compositions comprising the peptides of the invention, and diagnostic and therapeutic methods utilizing the peptides and pharmaceutical compositions of the invention.
39 Claims, 1 Drawing Figures

US PAT NO: 5,618,785 [IMAGE AVAILABLE] L3: 7 of 13

DETDESC:

DETD(65)

Tumor . . has been well described, suggesting a role for platelets in the spread of some cancers. Recently, it was reported that P-**selectin** binds to tumor cells in a variety of human carcinoma tissue sections (colon, lung, and breast), and that P-**selectin** binds to the cell surface of a number of cell lines derived from various carcinomas, but not from melanomas. Aruffo, . . . A., et al., Proc. Natl. Acad. Sci. USA, 89:2292-2296 (1992). Aruggo et al. also reference earlier work suggesting that E-**selectin** might be involved in tumor metastasis by mediating the adhesion of a colon carcinoma cell line (HT-20) to activated endothelial cells in vitro. Platelet-leukocyte interactions are believed to be important in **atherosclerosis**. Platelets might have a role in recruitment of monocytes into atherosclerotic plaques; the accumulation of monocytes is known to be. . .

US PAT NO: 5,605,821 [IMAGE AVAILABLE] L3: 8 of 13
DATE ISSUED: Feb. 25, 1997
TITLE: Expression control sequences of the P-selectin gene
INVENTOR: Rodger P. McEver, Oklahoma City, OK
Junhang Pan, Oklahoma City, OK
ASSIGNEE: Board of Regents of the University of Oklahoma, Norman, OK (U.S. corp.)
APPL-NO: 08/110,158
DATE FILED: Aug. 20, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 320,408, Mar. 8, 1989, Pat. No. 5,378,464.
INT-CL: [6] C12N 5/00; C07H 21/04
US-CL-ISSUED: 435/172.3, 69.1, 320.1, 325, 366, 367, 371, 372, 365; 536/23.1, 23.5, 24.1, 24.31; 935/16, 23, 34
US-CL-CURRENT: 435/172.3, 320.1, 325, 365, 366, 367, 371, 372; 536/23.1, 23.5, 24.1, 24.31; 935/16, 23, 34
SEARCH-FLD: 536/24.1, 23.5, 24.31, 23.1; 435/172.3, 69.1, 240.2, 320.1; 800/2; 935/6, 23, 34
REF-CITED:

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5,198,424	3/1993	McEver	514/13

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WO91/07993	6/1991 World Intellectual Property Organization
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PRIM-EXMR: Bruce R. Campell
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ABSTRACT:
DNA molecules and methods for the regulated expression of a gene in endothelial cells or megakaryocytes, are described, wherein the 5' flanking region of the P-selectin gene, or portions thereof, is ligated to the 5' end of a gene. The DNA molecules are also used as probes for screening individuals with abnormal levels of expression of P-selectin, or for production of pharmaceutical compositions to inhibit inflammation by inhibition of expression of P-selectin. These DNA molecules can also be used to identify and isolate previously unknown proteins which are involved in regulation of gene expression.

10 Claims, 10 Drawing Figures

US PAT NO: 5,605,821 [IMAGE AVAILABLE] L3: 8 of 13

DETDESC:

DETD(96)

The above methods and compositions may be used locally or systemically to inhibit the expression of P-**selectin** in vivo and thereby inhibit inflammation. The ability to inhibit or otherwise regulate the inflammatory response at a site is. . . damage include injury from ischemia and reperfusion, bacterial sepsis and disseminated intravascular coagulation, adult respiratory distress syndrome, tumor metastasis, and **atherosclerosis** Systemic administration of compounds to achieve chronic systemic down-regulation of P-**selectin** expression may also be useful, for example, in a chronic disorder such as rheumatoid arthritis.

US PAT NO: 5,602,307 [IMAGE AVAILABLE] L3: 9 of 13
DATE ISSUED: Feb. 11, 1997
TITLE: Non-human animal having predefined allele of a cellular adhesion gene
INVENTOR: Arthur L. Beaudet, Houston, TX
Raymond Wilson, Timonium, MD
Allan Bradley, Houston, TX
William E. O'Brien, Houston, TX
James Sligh, Houston, TX
Christie Ballantyne, Houston, TX
Daniel Bullard, Houston, TX

ASSIGNEE: Baylor College of Medicine, Houston, TX (U.S. corp.)
APPL-NO: 08/309,549
DATE-FILED: Sep. 20, 1994
REL-US-DATA: Continuation of Ser. No. 928,010, Aug. 12, 1992, abandoned.
INT-CL: [6] C12N 15/00; C12N 5/00; A61K 49/00
US-CL-ISSUED: 800/2; DIG.1; 424/9.2, 9.1; 435/172.3; 935/62
US-CL-CURRENT: 800/2; 424/9.1, 9.2; 435/172.3; 800/DIG.1; 935/62
SEARCH-FLD: 800/2, DIG.1; 435/172.3, 240.2; 424/9.1, 9.2; 935/62, 111
REF-CITED

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Gridley, T. et al., Trends Genet. 3:162 (1987).

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PRIM-EXMR: Jasemine C. Chambers
LEGAL-REP: Fulbright & Jaworski L.L.P.

ABSTRACT:

A transgenic mouse which contains a predefined, specific and desired alteration in at least one of its two chromosomal alleles of a cellular adhesion gene, such that at least one of these alleles contains a mutation which alters the expression of the allele

12 Claims, 12 Drawing Figures

US PAT NO: 5,602,307 [IMAGE AVAILABLE] L3: 9 of 13

SUMMARY

BSUM(76)

Despite [illegible] of agonists or antagonists of inflammation, they could also be used to identify agents capable of suppressing or preventing cancer, **atherosclerosis**, transplantation rejection, and autoimmune disease. For example, if mutations which reduce the expression of CD18, CD11a, CD11b, CD11c, VLA 4, ICAM 1, ICAM-2, VCAM-1, P-**selectin**, E-**selectin**, or L-**selectin**, protect an animal against **atherosclerosis**, transplantation rejection, inflammatory processes, tumor metastasis, or other disease processes, this would be strong evidence that drugs which block the [illegible]

US PAT NO: 5,580,722 [IMAGE AVAILABLE] L3: 10 of 13

DATE-ISSUED: Dec. 3, 1996
TITLE: Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease
INVENTOR: J. Gordon Foulkes, Huntington Station, NY
Franz E. Liechtfried, Vienna, Austria
Christian Peter, Vienna, Austria
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ASSIGNEE: Oncogene Science, Inc., Uniondale, NY (U.S. corp.)
APPL-NO: 07/832,905
DATE-FILED: Feb. 7, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 555,196, Jul. 18, 1990, abandoned, which is a continuation-in-part of Ser. No. 382,712, Jul. 18, 1989, abandoned.
INT-CL: [6] C12P 19/34; C12Q 1/68
US-CL-ISSUED: 435/6, 91.1, 91.2; 935/77, 78
US-CL-CURRENT: 435/6, 91.1, 91.2, 935/77, 78
SEARCH-FLD: 435/6, 91, 91.1, 91.2, 935/77, 78
REF-CITED

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WO89/02472	3/1989	World Intellectual Property Organization

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ART-UNIT: 187
PRIM-EXMR: Stephanie W. Zitomer
LEGAL-REP: John P. White

ABSTRACT:
The invention provided for a method of directly and specifically transcriptionally modulating the expression of a gene encoding a protein of interest associated with treatment of one or more symptoms of a cardiovascular disease such as atherosclerosis, restenosis or hypertension.
Further provided is a method of determining whether a molecule not previously known to be a modulator of protein biosynthesis is capable of directly and specifically transcriptionally modulating the expression of a gene encoding a protein of interest associated with treatment of one or more symptoms of a cardiovascular disease.
Lastly, the invention provides a method of directly and specifically transcriptionally modulating in a human being the expression of a gene encoding a protein of interest associated with treatment of one or more symptoms of a cardiovascular disease, thus ameliorating the disease.

7 Claims, 46 Drawing Figures

U.S. PAT. NO: 5,580,722 [IMAGE AVAILABLE] L3: 10 of 13

DETDESC:

DETD(45)

In the methods described above the cardiovascular disease may be **atherosclerosis** or restenosis. The protein of interest may be involved in lipid transport or cellular uptake e.g. apolipoprotein (a, AI, AII, . . . and chemotaxis e.g. CSF-1, CSF-1 receptor, monocyte chemoattractant protein-1 (MCP-1) or MCP-1 receptor. Lastly the protein of interest associated with **atherosclerosis** may be associated with endothelial cell adhesion such as VCAM-1, VLA-4 .alpha..sub.4 subunit, VLA-4 .beta..sub.1 subunit, **ELAM**-1, ICAM-1, LFA-1 .alpha..sub.L subunit, LFA-1 .beta..sub.2 subunit, GMP-140 (**PADGEM**), neuropeptide Y, VLA-4 .alpha. sub 1 subunit, vitronectin receptor or 13-hydoxyoctadeca-9,11-dienoic acid (13-HODE) receptor. The protein of interest associated with the treatment of cardiovascular disease or **atherosclerosis** may be PEPCK.

US PAT NO: 5,576,305 [IMAGE AVAILABLE] L3: 11 of 13
DATE ISSUED: Nov. 19, 1996
TITLE: Intercellular adhesion mediators
INVENTOR: Robert M. Ratcliffe, Carlsbad, CA
ASSIGNEE: Cytel Corporation, San Diego, CA (U.S. corp.)
APPL-NO: 08/466,040
DATE FILED: Jun. 6, 1995
REL-US-DATA: Continuation-in-part of Ser. No. 63,181, May 14, 1993, which is a continuation-in-part of Ser. No. 810,789, Dec. 17, 1991, abandoned, which is a continuation-in-part of Ser. No. 716,735, Jun. 17, 1991, abandoned, which is a continuation-in-part of Ser. No. 632,390, Dec. 21, 1990, abandoned, which is a continuation-in-part of Ser. No. 619,319, Nov. 28, 1990, abandoned, which is a continuation-in-part of Ser. No. 538,853, Jun. 15, 1990, abandoned.
INT-CL: [6] A61K 31/73; C07H 3/06
US-CL-ISSUED: 514/25; 54, 62; 536/17.2; 53, 55.2
US-CL-CURRENT: 514/25; 54, 62; 536/17.2; 53, 55.2
SEARCH-FLD: 514/25; 54, 62; 536/17.2; 53, 55.2
REF-CITED:

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5,378,464	1/1995	McEver	424/143.1

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ART-UNIT: 121
PRIM-EXMR: Gary L. Kunz
ASST-EXMR: Kathleen Kahler Fonda
LEGAL-REP: Townsend and Townsend and Crew LLP

ABSTRACT

The present invention is directed towards compositions and methods for reducing or controlling inflammation and for treating inflammatory disease processes and other pathological conditions mediated by intercellular adhesion. The compositions of the invention include compounds that selectively bind selectin receptors, the selectin binding activity being mediated by a carbohydrate moiety. The selectin-binding moieties of the invention are derivatives of a sialylated, fucosylated N-acetyllactosamine unit of the Lewis X antigen. Compounds containing a selectin-binding moiety in both monovalent and multivalent forms are included in the invention. The compounds of the invention are provided as pharmaceutical compositions which include, for example, liposomes that carry selectin-binding moieties of the invention.

8 Claims, 26 Drawing Figures

US PAT NO: 5,576,305 [IMAGE AVAILABLE] L3: 11 of 13

SUMMARY:

BSUM(19)

The . . . compositions are useful in methods of inhibiting intercellular adhesion in a patient for a disease process, such as inflammation. The **selectin** receptor, such as E-**Selectin** or P-**Selectin**, may be expressed on vascular endothelial cells or platelets. The inflammatory process may be, for example, septic shock, wound associated. . . . shock, nephritis, and acute and chronic inflammation, including atopic dermatitis, psoriasis, and inflammatory bowel disease. Various platelet-mediated pathologies such as **atherosclerosis** and clotting can also be treated. In addition, tumor metastasis can be inhibited or prevented by inhibiting the adhesion of.

DETDESC:

DETD(34)

All . . . variety of purposes, including, for example, competitive inhibition of the binding of SLe.sup.x-bearing cells to cells that express the **selectin** receptors. By binding of the compounds of the invention to a cell surface **selectin**, interaction of the **selectin** with the native SLe.sup.x ligand on migrating cells will be prevented, interfering with normal and pathological binding of leukocytes and other cells to the endothelium or platelets. Thus, compounds that contain one or more **selectin**-binding moieties can serve as effective inhibitors of, for instance, inflammation, **atherosclerosis**, clotting and other endothelial or platelet-mediated pathologies.

US PAT NO: 5,529,902 [IMAGE AVAILABLE] L3: 12 of 13
DATE ISSUED: Jun. 25, 1996
TITLE: Direct fluorescence conjugated immunoassay for platelet activation
INVENTOR: Bruce A. Kottke, Lakeland, FL
Deyong Wei, Rochester, MN
ASSIGNEE: Mayo Foundation for Medical Education and Research, Rochester, MN (U.S. corp.)
APPL-NO: 08/377,679
DATE FILED: Jan. 27, 1995
REL-US-DATA: Continuation of Ser. No. 142,766, Oct. 26, 1993, abandoned
INT-CL: [6] G01N 33/533; G01N 33/536; G01N 33/577
US-CL-ISSUED: 435/7.21, 28; 436/172, 536, 548, 530/388.1, 388.22
US-CL-CURRENT: 435/7.21, 28; 436/172, 536, 548, 530/388.1, 388.22
SEARCH-FLD: 435/7.21, 28; 436/172, 536, 548; 530/388.1, 388.22
REF-CITED:

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ART-UNIT: 182
PRIM-EXMR: Toni R. Scheiner
ASST-EXMR: Nancy J. Parsons
LEGAL REP: Schwegman, Lundberg & Woessner

ABSTRACT:
A method is provided to measure the extent of platelet activation by fluorometrically determining the extent of expression of P selectin in a platelet sample in vitro, using a maximally activated platelet sample as a reference standard.

20 Claims, 12 Drawing Figures

US PAT NO: 5,529,902 [IMAGE AVAILABLE] L3: 12 of 13

SUMMARY

BSUM(4)

Several . . . J. Clin. Invest., 78, 340 (1986) reported that platelet activation with accompanying alpha granule release can be ascertained by examining P-**selectin** expression. Thus, assays have been designed that combine the use of activation-specific monoclonal antibodies with flow cytometry. See, for example, R. E. Scharf et al., **Arteriosclerosis** and Thrombosis, 12, 1475 (1992). These assays can be performed on whole blood and can facilitate the detection of platelet.

DETDESC:

DETD(3)

TABLE I

Anti-P-**Selectin** Antibody	Label	Reference
S12	Fluorescein or phyoery-thrin	R. E. Scharf et al., **Arteriosclerosis** and Thrombosis, 12, 1475 (1992); R. P. McEver et al. J. Biol. Chem., 259, 9799 . . .

US PAT NO: 5,380,747 [IMAGE AVAILABLE] L3: 13 of 13
DATE ISSUED: Jan. 10, 1995
TITLE: Treatment for atherosclerosis and other cardiovascular and inflammatory diseases
INVENTOR: Russell M. Medford, Atlanta, GA
Margaret K. Offermann, Atlanta, GA
R. Wayne Alexander, Atlanta, GA
ASSIGNEE (Emory University, Atlanta, GA (U.S. corp.)
APPL-NO: 07/969,934
DATE FILED: Oct. 30, 1992
INT CL: [6] A61K 31/40; A61K 31/27
US-CL-ISSUED: 514/423, 210, 212, 315, 476, 477
US-CL-CURRENT 514/423, 210, 212, 315, 476, 477
SEARCH-FLD: 514/423, 476, 477, 478, 210, 315, 212
REF-CITED:

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ABSTRACT:
Dithiocarboxylates, and in particular, dithiocarbamates, block the induced expression of the endothelial cell surface adhesion molecule VCAM-1, and are therefor useful in the treatment of cardiovascular disease including atherosclerosis, post-angioplasty restenosis, coronary artery diseases, and angina, as well as noncardiovascular inflammatory diseases that are mediated by VCAM-1.

12 Claims, 15 Drawing Figures

US PAT NO: 5,380,747 [IMAGE AVAILABLE] 13 of 13

SUMMARY:

BSUM(3)

Adhesion of leukocytes to the endothelium represents a fundamental, early event in a wide variety of inflammatory conditions, including **atherosclerosis**, auto immune disorders and bacterial and viral infections. This process is mediated in part by the induced expression of endothelial cell surface adhesion molecules, such as ICAM-1 (intracellular adhesion molecule-1), VCAM-1 (vascular adhesion molecule-1) and **ELAM**-1 (endothelial leukocyte adhesion molecule-1). These adhesion molecules bind to immune cells, which initiate and propagate the inflammatory response. One of. . .